

C.F.R. §§ 1.825(a) and 1.821(c), and a copy of the Substitute "Sequence Listing" in computer readable form as required by 37 C.F.R. §§ 1.825(b) and 1.821(e).

As required by 37 C.F.R. § 1.825(b), Applicant's Attorney hereby states that the contents of the Substitute "Sequence Listing" in paper form and in the computer readable form submitted herewith are the same and, as required by 37 C.F.R. § 1.825(a), also states that the submission includes no new matter.

Please amend the above-identified application as follows:

In the Specification

Amendments to the specification are indicated in the attached "Marked Up Version of Amendments" (pages i - iii).

Please replace the paragraph at page 10, lines 4 through 28, continuing to page 11, lines 1 through 8 with the following paragraph:

Peptides, both D-peptides and L-peptides, which fit into a deep hydrophobic pocket in the trimeric N-helix coiled-coil of HIV-1 envelope glycoprotein gp41 are also the subject of this invention. The D-peptides are the first molecules that have been shown to bind exclusively to the gp41 hydrophobic pocket. The observation that these D-peptides inhibit gp41-mediated membrane fusion processes (syncytia formation and viral infection) provides the first direct demonstration that HIV-1 infection can be inhibited by molecules that bind specifically to pocket. The validation of the gp41 hydrophobic pocket as a drug target sets the stage for the development of a new class of orally bioavailable anti-HIV drugs, that work by inhibiting viral entry into cells. Such drugs would be a useful addition to the current regimen used to treat HIV-1 infection with combination therapies. D-peptides, such as the D-peptides described herein, portions, modification and variants thereof and larger molecules (e.g., polypeptides) which

comprise all or a portion of a D-peptide described herein, are useful to inhibit HIV membrane fusion and, thus, HIV entry into cells. D-peptides, corresponding to the D-amino acid version of phage sequences identified as described herein, are inhibitors of HIV-1 infection and syncytia formation. The C-terminal residues in these D-peptide inhibitors have the sequence pattern: CXXXXXEWXWLCAA-am (SEQ ID NO: 69). (In the phage-display library, the positions corresponding to the C residues were encoded as either C or S, the positions corresponding to the AA residues were encoded as such and the other 10 positions (indicated by X) were randomly encoded. The -am represents a C-terminal amide, added as part of the peptide synthesis procedure.) The N-terminal residues in the D-peptide inhibitors are, for example, ac-GA, ac-KKGA (SEQ ID NO: 70), or ac-KKKKGA (SEQ ID NO: 71). The ac- represents an N-terminal acetyl group added as part of the peptide synthesis procedure. The C-terminal amide and the N-terminal acetyl group are optional components of D-peptides of this invention. Other N-terminal residues can be included, in place of or in addition to those in the previous sentence, as desired (e.g., to increase solubility). For example, D-peptides of the following sequences are also the subject of this invention:

ac-XXCXXXXXEWXWLCXX-am (SEQ ID NO: 28);
ac-KKXXCXXXXXEWXWLCXX-am (SEQ ID NO: 29);
ac-KKKKXXCXXXXXEWXWLCXX-am (SEQ ID NO: 30);
ac-XXCXXXXXEWXWLCXXX-am (SEQ ID NO: 31);
ac-KKXXCXXXXXEWXWLCXXX-am (SEQ ID NO: 32); and
ac-KKKKXXCXXXXXEWXWLCXXX-am (SEQ ID NO: 33).

Please replace the paragraph at page 57, lines 4 through 20 with the following paragraph: